**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Patent Application No. 10/579,007

Confirmation No. 2230

Applicant: Panicali et al.

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Examiner: Anne Marie Sabrina Wehbe

Docket No.: 701278 (Client Reference No. E-088-2005/0-US-03)

Customer No.: 45733

**DECLARATION UNDER 37 C.F.R. § 1.132 OF JEFFREY SCHLOM, PH.D.**

I, Jeffrey Schlom, Ph.D., do hereby declare:

1. I am a co-inventor of the subject matter disclosed and claimed in the above-captioned patent application.

2. I am aware of the general knowledge available in the art and of the skill level of the ordinary artisan as it exists today and as it existed at the earliest priority date of the above-identified patent application (referred to herein as the "present application") of November 12, 2003.

3. I am familiar with the present application. The pending claims are directed to a method for inducing an immunological response against a cell expressing a breast cancer associated antigen in a human, wherein the method comprises (a) selecting a human having breast cancer or at risk for developing such a breast cancer tumor, (b) administering to the individual a first poxvirus vector containing one or more DNA segments that encode (i) mucin (MUC) or an antigenic portion thereof or modified version thereof and (ii) carcinoembryonic antigen (CEA) or an antigenic portion thereof or modified version thereof, and (c) at regular intervals thereafter administering at least a second poxvirus vector containing one or more DNA segments that encode (i) MUC or antigenic portion thereof or modified version thereof and (ii) CEA or an antigenic portion thereof or modified version thereof, such that an immunological response against the cell expressing the breast cancer associated antigen is induced in the individual.

4. I have reviewed the Office Action from the U.S. Patent and Trademark Office (USPTO) regarding the present application dated July 14, 2011. I understand that the USPTO has rejected the pending claims of the present application because the USPTO considers that the subject matter of the pending claims is obvious in view of the disclosures of Schlom et al. (WO 00/34494) and Pecher (WO 01/24832) when considered alone or in further combination with Grosenbach et al. (*Cancer Research, 61*: 4497-4505 (2001)).

5. None of the cited references discloses a method for inducing an immunological response against a cell expressing a breast cancer associated antigen in a human by administering a first and second poxvirus vector containing one or more DNA segments that encode (i) MUC or an antigenic portion thereof or modified version thereof, and (ii) CEA or an antigenic portion thereof or modified version thereof.

6. In my opinion, one of ordinary skill would not have known, based on the references cited in the Office Action, whether the administration of a first and second poxvirus vector containing one or more DNA segments that encode (i) MUC or an antigenic portion thereof or modified version thereof, and (ii) CEA or an antigenic portion thereof or modified version thereof would result in successfully inducing an immunological response against a cell expressing a breast cancer associated antigen, thereby inhibiting growth of a breast cancer cell in an individual.

7. The impact of administering two antigens together at one location could not have been known without extensive experimentation, such as by designing and implementing a clinical study or, at the very least, a mouse model system for breast cancer. As described by Palmowski et al. (*J. Immunol., 168*: 4391-4398 (2002)) and Brody et al. (*Immunol., 22*: 75-85 (1972)), the presentation of two antigens together (at the same location) could result in competition between the two antigens, thereby resulting in a reduced immune response to one or both of the antigens (see, e.g., page 4397, second column, fourth full paragraph, of Palmowski et al., and page 83, lines 1-3, of Brody et al.).

8. Clinical studies were performed to determine the effect of administering a vaccine comprising a first and second vector containing CEA and MUC (see Examples 4, 5, and 11 of the present application), as encompassed by the

pending claims. Several metastatic breast cancer patients receiving this vaccine were shown to have an increase in CEA and MUC-1 T cells and significant drop in the cytokines and chemokines produced mainly by tumor cells, corresponding with a clinical response (see page 7168, column 2, last full paragraph, of Mohebtash et al., *Clin. Cancer Res., 17(22)*: 7164-7173 (2011)). Additionally, a decrease in tumor volume was observed (see page 3067, column 1, first full paragraph, of Gulley et al., *Clin. Cancer Res., 14(10)*: 3060-3069 (2008)).

9. The inventive methods that employ a poxvirus vector encoding CEA and MUC result in the beneficial effect of stimulating the immune system to target both the CEA and MUC antigens without antigenic competition between the two tumor antigens (see page 1605, column 1, first full paragraph, of Tsang et al., *Clin. Cancer Res., 11*: 1597-1607 (2005)).

10. The unexpected beneficial results demonstrate that the inventive methods can successfully be used to induce an immunological response against breast cancer cells, thereby treating breast cancer.

11. I hereby declare that all statements made herein of my own knowledge are true, that all statements made on information and belief are believed to be true, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: 1-13-12

Jeffrey Schlom, Ph.D.